Summary of Safety and Effectiveness Data

I. General Information

Device Generic Name: Vascular hemostasis device

Device Trade Name: QuickSeal™ Femoral Arterial Closure System

Applicant's Name and Address: SUB-Q, Inc.
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San Clemente, CA 92673

Premarket Approval Application Number: P010049

Date of Panel recommendation: None

Date of Notice of Approval to Applicant: March 25, 2002

II. Indications for Use

The QuickSeal Femoral Arterial Closure System is intended for the delivery of Gelfoam for "extravascular" closure of femoral artery access sites. The system is indicated for use in reducing time to hemostasis, at femoral artery puncture sites and in reducing time to ambulation in patients who have undergone diagnostic or interventional procedures using 8 French or smaller procedural sheaths. The device reduces time to eligibility for hospital discharge in patients who have undergone diagnostic or interventional procedures and reduces time to actual hospital discharge in patients who have undergone diagnostic procedures

III. Contraindications

This product is not intended for intravascular use.
The QuickSeal should not be used in patients who have a sensitivity or allergy to porcine derived material.
The QuickSeal should not be used if posterior arterial wall puncture is suspected, as this may lead to bleeding complications.

IV. Warnings and Precautions

The warnings and precautions can be found in the QuickSeal Femoral Arterial Closure System labeling

V. Device Description

A. Materials and Configuration

This device system delivers a hydrated absorbable hemostatic foam material (Gelfoam) extravascularly to a femoral artery access site. The device system comes to the user as a kit packaged in a box. Inside the box are several items that are sterile inside their own individual packages.

The components of the system (Device Version 1.9) are:

- Gelfoam resorbable hemostatic sponge
- Single-use disposable 3cc syringe used to advance the Gelfoam to the distal end of the Introduction Catheter.
- Single-use disposable .025" J-tipped guidewire used as a transfer tool to guide the Depth Marker, Pusher and the Introduction Catheter containing the Gelfoam to the target site.
- Single-use disposable Depth Marker w/Depth Indicator ring used to identify and set the depth of the tract on the Introduction Catheter.
- Single-use disposable Introduction Catheter w/Depth Indicator ring
- Cutting Tab for uniform Gelfoam sizing
- Single-use disposable Pusher used to deploy and ensure the Gelfoam is left in place adjacent to the external vessel wall.
- Single-use disposable Hydration Chamber used to hydrate the Gelfoam with sterile saline. The Chamber Connector is used to connect the Hydration Chamber to the Introduction catheter.

B. Principals of Operation

The use of the device requires two trained persons. Manual compression is applied in conjunction with the use of the device.

The Cutting Tab is provided to cut the Gelfoam to size. The Gelfoam sponge is placed in the Hydration Chamber and is hydrated with sterile saline using the 3cc syringe. The hydrated Gelfoam is then staged in the Introduction Catheter to facilitate the delivery process.

The Gelfoam is delivered extravascularly into the arterial access site directly over a Guidewire by using a "pin and pull" technique. The placement of the Gelfoam is just proximal to the outer vessel wall of the arterial access site and is left in place to promote hemostasis at the arterial puncture site.

VI. Alternative Practices and Procedures

Alternative practices for achieving hemostasis of the femoral artery puncture site post-catheterization include manual compression, mechanical compression, collagen hemostasis devices, and percutaneous delivery of sutures to the femoral artery access site. Pressure dressings and sandbags are routinely used in combination with compression methods to control oozing.

VII. Marketing History

The QuickSeal™ Femoral Arterial Closure System has not been marketed in the United States or any foreign country.

VIII. Adverse Effects of the Device on Health

The QuickSeal Femoral Arterial Closure System was evaluated in a randomized controlled clinical investigation involving 398 patients within the U.S. The QuickSeal Device was compared to Manual Compression methods following interventional and diagnostic catheterization procedures with 8 Fr and smaller sheath sizes. Prior to enrollment of randomized patients, each site enrolled non-randomized QuickSeal run-in patients for training purposes. There were a total of eighty-one (81) patients enrolled as non-randomized QuickSeal run-in patients. Of the 398 randomized patients, 240 (60%) were randomized to QuickSeal and 158 (40%) were randomized to Manual Compression. Of the patients randomized to QuickSeal, 145 (60%) were interventional and 95 (40 %) were diagnostic. Of the patients randomized to manual compression, 100 (63%) were interventional and 58 (37%) were diagnostic.

One death was reported during the randomized investigation, which was determined not to be device-related. This patient was randomized to the QuickSeal device.

Closure method related adverse events seen in the clinical study were:

- Hematoma
- Bleeding requiring transfusion
- Pseudoaneurysm not requiring treatment
- Pseudoaneurysm requiring thrombin injection
- Retroperitoneal bleed

Potential complications of allergic reaction, adhesion formation, infection or abscess, foreign body reaction, wound dehiscence or vessel occlusion were not seen.

Table 1 summarizes the adverse events reported within the randomized investigation's 30-day follow-up period. Events are summarized by percentage of randomized patients experiencing the event during the clinical investigation.

Table 1: Incidence of all adverse events in randomized patients
Number (Percentage) of Patients with an Event

Description of Event	**QuickSeal** N= 240	**Manual Compression** N= 158	Difference [95% C.I.] (a)
Closure method related			
Vascular damage requiring repair	2 (0.8%) (d)	0 (0.0%)	(-100, 1.8)
Retroperitoneal bleed	1 (0.4%) (e)	0 (0.0%)	(-100, 1.8)
Hematoma	0 (0.0%)	1 (0.6%) (f)	(-100, 1.8)
Total	**3 (1.3%)**	**1 (0.6%)**	(-100, 2.2)
Non-closure method related			
Mild*****	23 (9.6%)	12 (7.6%)	
Moderate*****	4 (1.7%)	2 (1.3%)	
Severe*****	6 (2.5%)	4 (2.5%)	
Total	**33 (13.8%)**	**18 (11.4%)**	
Minor adverse events			
Hematoma (2cm – 6cm)	33 (13.8%)	13 (8.2%)	(-100, 10.7)
Hematoma > 6cm	4 (1.7%)	0 (0.0%)	(-100, 3.0)
Ecchymosis	17 (7.1%)	12 (7.6%)	(-100, 3.9)
Bleeding	5 (2.1%)	3 (1.9%)	(-100, 2.5)
Minor pseudoaneurysm requiring no intervention	1 (0.4%)	0 (0.0%)	(-100, 1.1)
Total Minor Complications :	**50 (20.8%)**	**24 (15.2%)**	(-100, 12.0)
Device Failure (b)	8 (3.3%)	N/A	
Procedure Failure (c)	5 (2.1%)	1 (0.6%)	

(a) 95% C.I. represents a one sided confidence interval of the true difference between the percentage of patients with complications (QuickSeal- Control)
(b) Device failure rate was defined as the number of patients in which hemostasis was not achieved using the QuickSeal device or a major complication occurred.
(c) Procedure failure rate was defined as the number of patients in which hemostasis was not achieved, or a major complication occurred.
(d) Both patients experienced a pseudoaneurysm requiring a thrombin injection.
(e) Patient experienced a hematoma requiring a transfusion (one unit of packed red blood cells).
(f) Patient experienced a 10 x 10 cm hematoma requiring a transfusion (two units of packed red blood cells).

*****As determined by the investigational site

IX. Summary of non-clinical Studies

Summary of Safety and Effectiveness Data

A. Bench and In Vitro Device Characterization Testing

Biocompatibility

Biocompatibility testing of the QuickSeal Delivery System was conducted in accordance with the FDA-modified matrix of ISO 10993-1, "Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing". The following tests were conducted: cytotoxicity, systemic toxicity, hemolysis, sensitization, irritation, and pyrogenicity. The results indicated that the QuickSeal Delivery System is non-toxic, non-hemolytic, non-irritant and non-pyrogenic.

The Gelfoam, syringe and guidewire were previously approved for commercial distribution.

Functionality

In vitro tests were conducted to characterize the mechanical performance of the QuickSeal Femoral Arterial Closure System. Results from the mechanical tests demonstrated that the QuickSeal Femoral Arterial Closure System performance was acceptable. The tests are summarized in Table 2.

Table 2.
QuickSeal FUNCTIONAL TEST TABLE

Bench Test	Purpose	Number of Test Units	Acceptance Criteria	Results
12 Fr Introduction Catheter – original design	To verify the safety and efficacy of the design of the Introduction Catheter	15	a)Visual discrepancies b) .122 pin gauge must pass through lumen of Introduction Catheter with ease (no binding). c) Vent Cap must remain attached to the tube of the Introduction Catheter when a pull force of 2.5 pounds is exerted d) Female Luer connector must stay attached to the tube of the Introduction Catheter when a 10 pound force is applied for 15 seconds	Pass
9 Fr Pusher- original design	To verify the safety and efficacy of the Pusher	15	a) Visually inspect parts for discrepancies b) A .035 Guidewire must pass through the lumen of the Pusher easily without binding. c) The Female luer connector must stay attached to the Pusher shaft when a 5 pound force is applied for 15 seconds	Pass
System Design Verification- original design	To verify the safety and efficacy of the Irrigation	15	a) Visually inspect parts for discrepancies b) No leaks are present at the male/female luer connections when a 50 psi is applied	Pass

	Syringe System (Hydration Chamber and connectors)		using a 3cc syringe filled with distilled water for 10 seconds.	
Depth Marker- original design	To verify the safety and efficacy of the Depth Marker	15	a) Visually inspect parts for discrepancies b) A .035 diameter Guidewire must pass through the lumen of the Depth Gauge easily without binding.	Pass
Foam Cutter	To verify the safety and efficacy of the new cutter device for use with the QuickSeal Femoral Arterial Closure System	30	a) Gelfoam (3 samples) cut using the new Foam Cutter must be the same size and exhibit similar edges as the Gelfoam cut with the previous cutting device/template. b) The Foam Cutter is to remain attached to the Presentation Card when a 6-pound pull force is applied.	Pass
Depth Marker – design change Note: Because of the addition of the insert molded handle, a pull force and bend test was incorporated into the design verification to assure that the molding process does not weaken the shaft and that the handle is securely attached to the shaft.	To verify the safety and efficacy of the modified Depth Marker with an insert molded handle	30	a) Bend the tube (body) of the Depth Marker approximately 30 degrees. Verify the tube flexes without kinking or fracturing. b) A .035 Guidewire shall pass through the lumen of the Depth Marker easily, without friction. c) Verify the handle of the Depth Marker can withstand a 5-pound pull force without separating from the tube.	Pass
Introduction Catheter – design change Note: Because of the addition of an insert molded handle, a pull force was incorporated into the design verification to assure that the handle is securely attached to the shaft. The change to thermal forming of the distal end of the cannula requires a test	To verify the safety and efficacy of the modified Introduction Catheter with an insert molded handle and tip formed end	30	a) Following the Instructions for Use, prepare, hydrate and stage the Gelfoam pledget. Verify the Introduction Catheter functions as described in the IFU and that there are no leaks or separations of the components/connectors. b) Expose the Introduction Catheter/Vent Cap connection to 200-psi pressure and hold for 5 seconds, staging the Gelfoam pledget. Verify the vent cap remains attached to the Introduction Catheter during staging. c) Verify there are no leaks at the luer cap attachment point of the Introduction Catheter when exposed to 50 psi.	Pass

to assure that no leaks are present during foam staging and also requires a pressure test to ensue that the interface fit between cap/cannula can withstand normal use of the system during staging.			d) Verify the handle can withstand a minimum of 3 pounds of pull force without separating from the shaft.	
System Irrigation Design Verification – design change Note: The change to a removable chamber luer that mechanically attached to the proximal end of the hydration chamber requires a leak test and hydraulic pressure test to ensure the o-ring seals and the mechanical engagement can withstand the hydration and staging foam operations required by the system.	To verify the safety and efficacy of the chamber luer when used with the hydration chamber.	30	a) Visually inspect the units for defects, such as cracking. Cracking would indicate a failure. b) Pressurize the hydration chamber with the chamber luer attached to 200 psi. and hold for 5 seconds. Verify the chamber does not leak and the luer remains attached to the chamber body. c) Prepare, hydrate and stage the Gelfoam, following the Instructions for Use.	Pass
QuickSeal System Design Verification – design change – pre-assembled device Note: The change to a pre-assembled device with a mechanical/interference fit between the distal end of the cannula and the hydration chamber luer requires leak testing, hydraulic pressure testing that simulate actual hydration and staging of the foam.	To verify the safety and efficacy of the QuickSeal Femoral Arterial Closure System when pre-assembled.	30	a) Introduction Catheter and Hydration Chamber remain attached during staging b) Gelfoam hydrates as in previous design.	Pass

Sterilization and Shelf Life

The device is packaged as a kit in a Tyvek pouch. Several components are purchased as sterile by the sponsor from outside sources; the Gelfoam resorbable hemostatic sponge, single-use 3 cc disposable syringe and single-use 0.025" disposable J-tipped guidewire. The QuickSeal Delivery System is sterilized using EtO. The sponsor has provided a statement of conformance with standards for EtO residuals.

This device has been approved with a 6-month shelf life after review of the sponsor's 6-unit visual inspection protocol of shipping/handling.

B. Pre-Clinical Animal Studies

Preclinical animal studies

Animal studies were performed using the porcine model in both non-heparinized and heparinized animals. The studies were performed at two academic institutions with the assistance of SubQ personnel.

The QuickSeal Femoral Arterial Closure system was used on a punctured femoral artery accessed using the standard Seldinger technique. Seven animals were studied and 13 femoral arteries were studied. The device could be used in all 13 arteries.

The study was organized into two distinct chronic periods: 24-48 hours and 14-21 days. Six data points in three animals were acquired for the 24-48 hours period at one center and seven data points in 4 animals were acquired for the 14-21 days period at the other center.

Endpoints evaluated:

- **Time to hemostasis** (TTH) – determined by direct observation
- **Angiography**, using the carotid artery accessed by a cut down, was performed at 24 hours and 14-16 days post-procedure **to determine vessel patency.**
- **Histopathology** was performed of the puncture site and of the perivascular and subcutaneous tissue.

The average time to hemostasis in both chronic periods was 1 minute. No abnormal behavior or changes in the physical characteristics of any limb were recorded throughout the chronic period.

Angiography examinations of post 24 hour and 14-16 day chronic periods showed complete vessel patency with no signs of intravascular delivery or vessel extravasation.

Histopathology of the blood vessels did not show any documentation of vessel obstruction. There were several instances of mild endothelial loss documented.

X. Clinical Studies

The QuickSeal Femoral Arterial Closure System was evaluated in a randomized controlled multi-center clinical investigation involving 398 patients within the U.S. The QuickSeal Device was compared to Manual Compression methods following interventional and diagnostic catheterization procedures with 8 Fr and smaller sheath sizes. Prior to enrollment of randomized patients, eighty-one (81) patients were enrolled as non-randomized QuickSeal run-in patients.

The study was conducted at 10 U.S. institutions from July of 2000 to June of 2001. Only 9 sites enrolled patients. A 3:2 device-to-control randomization was used with randomization stratified according to type of procedure (interventional or diagnostic). Of the 398 randomized patients, 240 (60%) were randomized to QuickSeal and 158 (40%) were randomized to Manual Compression. Of the patients randomized to QuickSeal, 145 (60%) were interventional and 95 (40 %) were diagnostic. Of the patients randomized to manual compression, 100 (63%) were interventional and 58 (37%) were diagnostic.

There were wide differences in the numbers of patients enrolled per investigational site, which is shown in detail in Table 3. 91% of the QuickSeal patients were enrolled at four centers. The QuickSeal device was used after diagnostic procedures at 5 sites.

Table 3. Randomized patient enrollment by site

Site	QuickSeal			Manual Compression		
	Diagnostic N=95	**Therapeutic** N=145	**Total** N=240	**Diagnostic** N=58	**Therapeutic** N=100	**Total** N=158
1	10	13	23	6	9	15
2	22	23	45	15	15	30
3	46	39	85	27	29	56
4	4		4	1		1
5	13	53	66	8	33	41
6		11	11	1	8	9
7		3	3		3	3
8		1	1		1	1
9		2	2		2	2

The study was designed as an equivalency trial for the 30-day primary safety endpoint of the combined rate of major complications, and as a superiority trial for the primary effectiveness endpoints of time to hemostasis (time from the end of the antecedent procedure to the time hemostasis is first observed), and time to ambulation (time from the end of the antecedent procedure to the time patient stands at bedside and walks 10 feet). Major complications were defined as surgery or ultrasound-guided compression for vascular repair, bleeding requiring transfusion, groin-related infection requiring IV antibiotics or extended hospitalization.

Secondary endpoints included: the time to hospital discharge (the time the antecedent procedure ends and the time the patient is discharged from the hospital), the time a patient is deemed eligible for discharge (the time the antecedent procedure ends and the time at which the patient is deemed eligible for discharge relative to the access site closure).

Additional endpoints include procedure success rate and device success rate. Procedure success rate was defined as the number of patients in which hemostasis was achieved with freedom from major complications vs. the number attempted. Device success rate was defined as the number of patients in which hemostasis was achieved using the QuickSeal device with freedom from major complications.

Inclusion and Exclusion Criteria

Patients were enrolled if they met the following criteria: the patient was between 18 and 80 years of age; patient or guardian provided written informed consent, and; in a subgroup, patient agreed to an ultrasound examination of the femoral artery.

Patients were excluded from the investigation if they met any one of the following criteria:

- an arterial introducer sheath size of >8F;
- arterial closure site depth is <3 cm or >7.5 cm;
- pre-existing autoimmune disease;
- ipsilateral arterial site closure with QuickSeal device or manual compression within previous 6 weeks, or closure with another closure device within 180 days;
- pregnant or lactating;
- significant bleeding or platelet disorders including Thrombocytopenia (with <100,000 platelet count), Von Willebrand's disease, anemia (Hgb <10 gm/dl, Hct <30) and thrombasthenia;
- uncontrolled hypertension (blood pressure not controllable to <170/100 mm Hg);
- Bleeding pre- or post-sheath removal;

- Elevated ACT levels in the manual compression group >180 seconds, and in the QuickSeal group of >300 seconds for patients not receiving GP IIb/IIIa platelet inhibitors and >250 seconds for patients receiving GP IIb/IIIa platelet inhibitors.

Methodology

The following methodology was used at each of the investigational sites:

- Informed consent and baseline medical histories were obtained prior to the catheterization procedure.
- Sheath removal was based on ACT level. Sheaths were removed in the Manual Compression group when the ACT level was ≤180 seconds. Sheaths were removed in the QuickSeal group when the ACT level was ≤ 300 seconds for patients not receiving GP IIb/IIIa platelet inhibitors, and ≤250 seconds for patients receiving GP IIb/IIIa platelet inhibitors.
- The times when hemostasis, ambulation, discharge and eligible for hospital discharge occurred were recorded and the elapsed times to hemostasis, ambulation, hospital discharge and eligible for discharge were calculated from the end of the antecedent diagnostic or interventional procedure.
- Patients were followed in the hospital and at the 30-day follow clinical evaluation for evidence of major complications or other vascular complications. Femoral artery ultrasounds were performed at the follow-up visit on 221 patients for evidence of pseudoaneurysms and arterio-venous (AV) fistulae.

Study Population

There was no significant difference between the two randomized groups with respect to age, risk factors, peri-procedural medications, arteriotomy depth, or blood pressure.

Table 4. Patient Characteristics

	Age	Height	Weight	Peripheral vascular disease	Diabetes	Claudication and/or no distal pulse	Hypertension
QuickSeal	62	171cm	88 kg	25%	32%	26%	45%
Control	61	171cm	83 kg	24%	32%	23%	44%

Treatment variables

Access site – right femoral artery in 197 (82%) device and 133 (84%) control

GP IIb/IIIa inhibitor use – total of 96 patients

53 device or 22%

43 control or 27%

Heparin – 248 (62%) of the randomized
146 (61%) device
102 (65%) control

Table 5.
ACT at time of sheath pull

	Device		Control	
	Range	**Average (SD)**	**Range**	**Average (SD)**
Diagnostic procedure	94-298	141.1 (36.6)	87-186	134.1 (24.6)
Interventional procedure	104-300	217.2 (48.8)	114-299	160.9 (24.8)
Overall	94-300	187.0 (57.9)	87-299	150.6 (27.9)

Arterial sheath sizes were comparable between arms, as seen in Table 6.

Table 6. Sheath size

	Device	Control
5Fr	26%	23%
6Fr	39%	41%
7Fr	13%	15%
8Fr	23%	20%

Gender Bias Analysis
A higher number of male patients were enrolled in the study (65%) male vs. (35%) female, which is a reflection of the general referral pattern for patients undergoing interventional and diagnostic procedures. Both sexes had a statistically significant decrease in both time to hemostasis and time to ambulation.

Table 7. Primary effectiveness endpoint data
Per sex

	Time to hemostasis (minutes)				Time to ambulation (hours)			
	Diagnostic catheterization		Interventional catheterization		Diagnostic catheterization		Interventional catheterization	
	Device	**Control**	**Device**	**Control**	**Device**	**Control**	**Device**	**control**
Men								
n	60	31	96	71	60	31	96	71
median	15	31	15	175	1.4	5.5	4.3	10
mean	17.4	34.3	20	203	2.3	5.8	5.7	11.7
range	5-48	5-71	5-167	10-936	.9-16.2	4.1-8.9	1.1-21.5	4.3-22.3
Women								
n	35	27	49	29	35	27	49	29
median	16	28.5	15	127.5	1.5	6.2	4.4	9.4
mean	16.2	33.5	19	149	2.4	6	9.25	12.2
range	5-30	13-85	6-82	16-734	1-9	4.2-9.9	1.1-94.1	6.2-24.6

Summary of Safety and Effectiveness Data

Safety Data

A summary of the adverse events (complications) experienced by patients enrolled in the QuickSeal Femoral Arterial Closure System clinical investigation is reported in Table 1. Major complications were experienced by 3 (1.3%) of 240 patients randomized to the QuickSeal device compared to 1 (0.6%) of the 158 patients randomized to Manual Compression.

In 2 (0.8%) of the QuickSeal cases the Depth Marker went beyond the arteriotomy failing to measure the depth of the arteriotomy. In each case the procedure was successfully converted to manual compression prior to utilizing the QuickSeal delivery system with no complications. One (0.4%) of the QuickSeal cases was identified as a device failure for not achieving hemostasis. The procedure was converted to Manual Compression and a small (< 6 cm) hematoma developed with no further complications. Device malfunctions were not associated with any risk of major complications as compared to all other QuickSeal-treated patients.

No deaths were determined to be device-related. One death occurred in the QuickSeal arm during the 30-day follow-up period and was reported as not associated with the arterial access site closure.

Effectiveness Data

In both the diagnostic and interventional groups, use of the QuickSeal resulted in statistically significant decreases in time to hemostasis, time to ambulation, and the time a patient is deemed eligible for hospital discharge as compared to Manual Compression (Tables 2 and 3). In the diagnostic group there was a statistically significant decrease in time to actual discharge.

Summary of Safety and Effectiveness Data

Table 2: Overall Effectiveness Table

	QuickSeal n=240		Manual Compression n=158		p-value
	Mean (SD)	**Median**	**Mean (SD)**	**Median**	
Time to Hemostasis (min)	18.5 (14.4)	15.0	131.6 (159.2)	67.5	<0.001
Time to Ambulation (hours)	5.1 (8.2)	4.2	9.6 (5.1)	5.1	<0.001
Time to Discharge (hours) Eligible	6.6 (8.3)	4.9	15.4 (58.1)	9.0	<0.001
Time to Discharge (hours) Actual	26.2 (43.7)	20.6	36.3 (81.3)	22.2	0.006
Device Success (a)	232/240 (96.7%)		N/A		N/A
Procedure Success (b)	235/240 (97.9%)		157/158 (99.4%)		0.409

(a) Device failure rate was defined as the number of patients in which hemostasis was not achieved using the QuickSeal device or a major complication occurred.
(b) Procedure failure rate was defined as the number of patients in which hemostasis was not achieved, or a major complication occurred.
The number of patients is less than the total number of patients studied due to missing data for some patients.
There were no malfunctioning QuickSeal devices.

Table 3: Effectiveness Table by procedure type

	Diagnostic			Interventional		
	QuickSeal	**Manual Compression**	**p-value**	**QuickSeal**	**Manual Compression**	**p-value**
	Mean (SD) **Median** Range	Mean (SD) **Median** Range		Mean (SD) **Median** Range	Mean (SD) **Median** Range	
Time to Hemostasis (min)	17 (7.8) **15** 5-48	33.9 (17.9) **29** 5-85	<0.001	19.5 (17.4) **15** 5-167	187.8 (176.5) **176.5** 10-936	<0.001
Time to Ambulation (hours)	2.3 (2.2) **1.5** 0.9-16.2	5.87 (1.34) **5.8** 4.1-9.9	<0.001	6.9 (10) **4.4** 1.1-94.1	11.8 (5.2) **10** 4.3-24.6	<0.001
Time to Discharge (hours) Eligible	4.0 (3.9) **3.2** 1.1-27.2	6.6 (1.4) **6.4** 4.6-10.9	<0.001	8.3 (9.9) **6.2** 1.1-94.1	20.4 (72.6) **11.4** 4.5-733.3	<0.001
Time to Discharge (hours) Actual	22.7 (50.6) **4.3** 1.8-298.8	24.1 (42.9) **7.1** 4.6-213.7	<0.001 (a)	28.5 (38.6) **22.7** 3.1-436.1	43.5 (96.4) **23.3** 6.5-890.3	0.096

(a) P-Value is based on Wilcoxon Rank Sum Test. The time to discharge results for the diagnostic group are skewed to high values, as evidenced by the large difference between the mean and the median in both treatment groups. While the

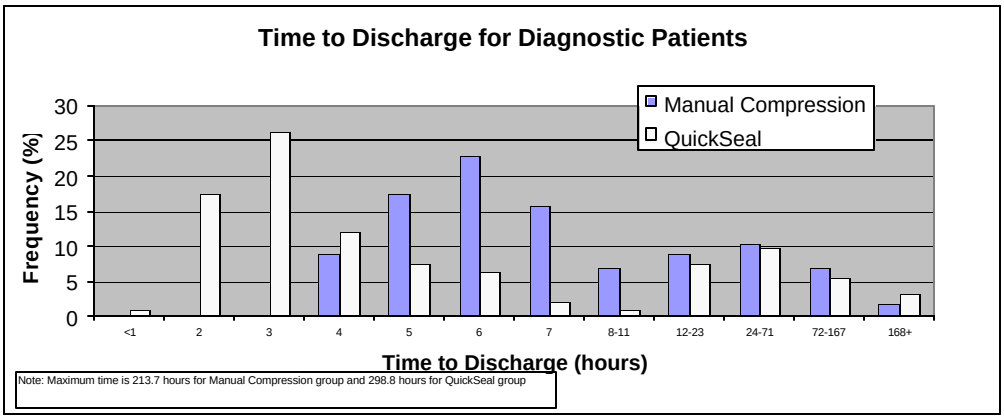
range for the QuickSeal diagnostic patients is 1.8-298.8 hours, 81.5% (75/92) of patients were discharged within 24 hours and 91.3% (84/92) of patients were discharged within 72 hours. Similarly, in the manual compression group, the range was 4.6-213.7 hours, with 80.7% (46/57) of patients being discharged within 24 hours and 91.2% (52/57) of patients being discharged within 72 hours. The skewed nature of this data necessitates the use of a non-parametric test, such as the Wilcoxon Rank Sum Test used above. This test is highly significant ($p<0.001$), which reflects the large difference in median time to discharge between the two groups (4.3 hours for QuickSeal versus 7.1 hours for manual compression).

Time to hemostasis is defined as the interval (in minutes) between the time the interventional or diagnostic procedure ends and the time at which hemostasis is achieved. Hemostasis is defined as the absence of bleeding and the absence of a palpable hematoma at the access site.

Time to ambulation is defined as the interval (in hours) between the time the interventional or diagnostic procedure ends and the time at which the patient walks 10 feet.

Time to discharge (eligible) the interval (in hours) between the time the interventional or diagnostic procedure ends, and the time the patient is deemed eligible for discharge from the hospital based solely on the hemostasis results.

Time to discharge (actual) the interval (in hours) between the time the interventional or diagnostic procedure ends, and the time the patient was actually discharged from the hospital.



XI. Conclusions Drawn from Studies

Results of the in vitro, animal studies, and clinical investigations provide valid scientific evidence and reasonable assurance that the QuickSeal Femoral Arterial Closure System is safe and effective when used in accordance with its labeling. The safety of the device has been demonstrated by the fact that the incidence of major complications in the randomized clinical investigation was equivalent for both treatment arms (QuickSeal Femoral Arterial Closure System procedure compared to Manual Compression therapy). The effectiveness of the QuickSeal Femoral Arterial Closure System was demonstrated by a significant reduction in the time to hemostasis and time to ambulation in both diagnostic and interventional patients treated with QuickSeal compared to those treated with standard Manual Compression.

The effectiveness of the QuickSeal Femoral Arterial Closure System was also demonstrated by a significant reduction in time to hospital discharge after a diagnostic cardiac catheterization and the time a patient is deemed eligible for hospital discharge in patients treated with the QuickSeal Femoral Arterial Closure System compared to those treated with standard Manual Compression.

XII. Panel Recommendations

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in this PMA substantially duplicates information previously reviewed by the panel.

XIII. FDA Decision

FDA issued a PMA approval letter to SUB-Q, Inc. on March 25, 2002.

The applicant's manufacturing facilities were inspected and found to be in compliance with the Quality Systems Regulation (21 CFR 820).

XIV. Approval Specification

Instructions for Use: See the labeling

Hazards to Health from the use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events section of the labeling.

Post-approval Requirements and Restrictions: See approval order.